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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/506,936	06/06/2005	Motowo Nakajima	PC/4-32388A	6976

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EXAMINER	
STONE, CHRISTOPHER R	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
12/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/506,936	NAKAJIMA ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER R. STONE	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,8 and 9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2, 5, 8 and 9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed September 18, 2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Status of Claims

Claims 2, 5, 8 and 9 are currently pending and under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 5, 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of pancreatic and cervical cancers/tumors, does not reasonably provide enablement for the treatment of other cancer/tumors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Claims 2, 5, 8 and 9 are drawn to a method of treating cancer/tumors comprising administering radiotherapy or cytotoxic therapy in combination with heat shock and further comprising the administration of N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl)-amino]-3- methylbutanamide hydrochloride . The prior art indicates that cancer

is a group of maladies not treatable with one medicament or therapeutic regimen. No single chemotherapeutic drug is useful for the treatment of every case of cancer. In fact, some types of cancer do not respond well to any known chemotherapeutic drugs (see Oxford Textbook of Oncology, p. 451, Column 2, last paragraph). These negative results indicate a lack of predictability in the art. Furthermore the Applicant has provided no working examples demonstrating the efficacy of this treatment on cancers, other than pancreatic and cervical cancer. For these reasons, it would take undue experimentation by one of ordinary skill in the art to use this method to treat cancers, other than pancreatic and cervical, with a reasonable expectation of success.

Applicant cites the legal standard with regard to the enablement requirement (all factors of which were considered when making the above enablement rejection) and then states that in light of said legal standard the instant claims are enabled (p. 6 and 7 of the response filed September 18, 2008). This is an allegation without factual support and is therefore unpersuasive. It would take undue experimentation by one of ordinary skill in the art to practice the instantly claimed invention for the reasons noted above. Routine experimentation requires reasonably predictable results. In the instant case, the treatment of every case of cancer with a single regimen is unpredictable, as noted above. One of ordinary skill in the art would not expect a reasonable correlation between the narrow disclosure of the instant specification (the treatment of pancreatic and cervical tumors) and the broad instant claims (the treatment of all cancer) because of the tremendous art recognized unpredictability with regard to the treatment of every case of cancer with a single regimen.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2, 5, 8 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macpherson et al (WO 96/40101), in view of Evans et al, further in view of Kouloulias et al.

Claims 2, 5, 8 and 9 are drawn to a method of treating cancer comprising administering cytotoxic therapy in combination with heat shock and further comprising the administration of N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl)-amino]-3-methylbutanamide hydrochloride and a package comprising N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl)-amino]-3- methylbutanamide hydrochloride and instructions for its use.

Macpherson et al teaches N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl)-amino]-3- methylbutanamide hydrochloride as a matrix metalloproteinase inhibitor, useful in the treatment of cancer (p. 16, paragraph 6 and p. 28, example 1a). Macpherson et al does not teach the use of N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl)-amino]-3- methylbutanamide hydrochloride in combination with cytotoxic therapy and heat shock therapy to treat pancreatic cancer. Evans et al teaches that matrix metalloproteinase inhibitors are useful in the treatment of pancreatic cancer (p. 1865, abstract, especially last sentence). Kouloulias et al teaches that chemotherapy in combination with hyperthermia (chemohyperthermia) is particularly advantageous for the treatment of pancreatic cancer, relative to other regimens (p. 564, abstract, Conclusions heading). Therefore it would have been obvious to one of ordinary skill in the art at the time of the instantly claimed invention to treat pancreatic cancer by administering chemotherapy and N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl)-amino]-3- methylbutanamide hydrochloride in combination with heat shock therapy since this multimodality therapy was known to be useful in the treatment of pancreatic cancer and N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl)-amino]-3- methylbutanamide hydrochloride was known to be useful for the same purpose, thus resulting in the practice of the instantly claimed invention with a reasonable expectation of success. In the instant case the idea of combining the treatments flows logically from their having been taught individually to be useful for the same purpose (i.e. the treatment of pancreatic cancer) in the prior art. Additionally, it would have been obvious to one of ordinary skill in the art at the time of

the instantly claimed invention to package an oral (enteral) dosage form of N-hydroxy-2(R)-[[4-methoxyphenylsulfonyl](3-picolyl)-amino]-3- methylbutanamide hydrochloride with instructions for its use in the aforementioned multimodality therapy, since the prior art renders the therapy itself obvious and this packaging and oral dosage forms are common in the pharmaceutical art for distribution and accurate and convenient administration of a drug/regimen.

Applicant argues that none of these references teach or suggest the instantly claimed method and composition. This is found unpersuasive because, as noted above, Kouloulias et al teaches that chemotherapy in combination with hyperthermia (chemohyperthermia) is particularly advantageous for the treatment of pancreatic cancer, relative to other regimens and Macpherson et al and Evans et al teach the instantly claimed compound as a member of a class of drug that is useful for the same purpose providing motivation to one of ordinary skill in the art to combine the treatments, since they were both known to be useful for the same purpose.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER R. STONE whose telephone number is (571)270-3494. The examiner can normally be reached on Monday-Thursday, 7:30am-4:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

09December2008
CRS

/Patricia A. Duffy/
Primary Examiner, Art Unit 1645